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274* Recurrent pancreatitis among cystic fibrosis (CF) patients at Stockholm CF Centre. Correlations with genotype

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Pancreatitis occurs mostly in CF patients with normal or reduced pancreatic function. Previous studies have revealed associations between CFTR mutations as well as SPINK1 variants and pancreatitis.

Objectives: To determine the frequency of pancreatitis among CF patients attending Stockholm CF Centre and relate symptoms to laboratory findings/genotype.

Methods: Patient records were examined regarding pancreatitis, genotype (CFTR and SPINK1), MR imaging and treatment. Pancreatitis has occurred in 5 of 230 CF patients (4 M). Mean age at diagnosis of pancreatitis was 25.2 (20–35) yrs. All patients were diagnosed having CF as adults except one (2 yrs of age). Two patients were pancreatic sufficient and 3 were partially insufficient. Their CFTR genotypes were: F508del/I506L, R117C/F5508del, S549I/S549I, S945L/T1086I, F508del/Y109N. One of them also has a SPINK1 variant (homozygocity for c.101A>G:p.Asn34SER), associated with pancreatitis in non-CF populations. All patients have been treated with oral mucolytics, pancreatic enzymes and UDCA during different periods of time and with varying results. However, a lower frequency of pancreatitis after having received the CF diagnosis and appropriate treatment was seen in those diagnosed having CF as adults.

Conclusion: In our total CF patient population 2.2% had evidence of recurrent pancreatitis. The occurrence of SPINK1 variations in the Stockholm material is in progress. The only patient who so far has been shown to have SPINK1 variation is actually the youngest one having had pancreatitis. The result of the medications used is hard to evaluate due to the small number of patients, but in one case the effect of UDCA was convincing.

275 Evaluation of cystic fibrosis (CF) liver disease and the indication and effect of ursodeoxycholic acid in a Dutch CF patient cohort

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Aim: To determine indications for starting ursodeoxycholic acid (UDCA) in our adult cystic fibrosis (CF) population, to evaluate its effect on liver disease and to relate liver cirrhosis to different CF genotypes.

Methods: The use of UDCA was evaluated retrospectively in 166 adult CF patients in 2010. Of these patients liver biochemistry tests and ultrasonographic findings were collected from medical records before and after the start of UDCA.

Results: One hundred nine of the 166 patients had undergone an ultrasound (US). Cirrhosis was present in 21.1% (23/109) and 3.7% (4/109) had both cirrhosis and portal hypertension. In our population 44 patients used UDCA. The most common indication for the start of UDCA was an increase in one or more liver enzymes (AST, ALT, AST) in combination with ultrasonographic abnormalities (68.2%; 30/44). Based on Colombo et al. 56.8% of participants are entitled to UDCA therapy. There was no relation between increased serum liver enzymes and evidence of cirrhosis on US before the start of UDCA. The levels of AST, ALT, and GGT were significantly lower after UDCA treatment compared to the levels before starting UDCA. Of the 23 patients with cirrhosis twenty patients had two severe CFTR mutations.

Conclusion: In literature there is little evidence for the indication to start UDCA. In our population UDCA was started mainly based on raised liver enzymes and ultrasonography abnormalities. Serum liver enzymes are poorly predictive for the presence of cystic fibrosis related liver disease (CFLD). Therefore ultrasonography of the liver should be part of the screening for liver disease. A severe genotype could be a possible risk factor for developing CFLD.

276* Long-term pulmonary outcome in cystic fibrosis (CF) is not adversely affected in CF associated liver disease treated with UDCA

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Objective: To define long-term pulmonary outcome in CF patients affected by liver disease and treated with ursodeoxycholic acid (UDCA).

Methods: In a retrospective analysis, average annual FEV1 values of all consecutive cases since 1989 of CF patients affected by liver disease with serum liver enzyme elevation >1.5 upper normal limit >6 months and/or persistent liver enlargement, all under UDCA treatment, were compared to gender and age matched controls.

Patients: From our cohort of 382 CF patients, 98 cases (56 males) and 98 contemporary controls with a mean age at the beginning of the observation of 14.8 years (range 0.6–36) and 13.3 years (0.5–34) respectively and a mean duration of observation 7.2 years (1–15) and 7.4 years (1–15) respectively were included as study population.

Results: Loss of lung function over time was not different between the cases and controls. Average loss of FEV1 was −1.36/year (±1.86) for the patients with liver disease and treated with UDCA and −0.94/year (±1.98) for the matched controls ($p = 0.388$ in Wilcoxon signed rank test). Similar results were obtained with the exploratory t-test for paired samples ($p = 0.335$) and unpaired comparisons (Wilcoxon-Mann-Whitney $p = 0.253$).

Conclusion: CF associated liver disease treated with UDCA therapy does not negatively affect long-term pulmonary outcome in CF patients. CF patients affected by liver disease had a stable lung function over a long observation period, comparable to that of CF patients not affected by liver disease.

277* Outcome following lung transplantation for patients with cystic fibrosis related liver disease: a single centre experience

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Uncertainty remains over the impact of cystic fibrosis related liver disease (CFRLD) in the context of lung transplantation. We compared outcome following transplantation in patients with and without CFRLD.

A retrospective case note and database review was conducted. Those with significant CFRLD at assessment (defined as persistently deranged liver function tests, liver ultrasound abnormalities and the use of ursodeoxycholic acid) were identified. No subjects had significant disturbance of synthetic function.

A total of 238 patients underwent lung transplantation for CF (1989–2010). 62 had significant CFRLD at assessment. Overall survival was 82% at 1 year, 62% at 5 years and 51% at 10 years. There was no significant difference in survival between the two groups ($p = 0.47$). In the CFRLD cohort, mean bilirubin at assessment was 6.37 and 8.3 at 1 year ($p = 0.0003$: a significant rise but values within normal limits). Mean ALT did not change significantly ($p = 0.97$) and mean ALP fell from 162 to 146 ($p = 0.0004$). Of the 62 with CFRLD, 31 had evidence of portal hypertension on ultrasound and the remainder fatty liver or coarse echogenicity. 24 had an ultrasound scan recorded post transplantation; none showed evidence of progression. Follow-up revealed 1 death from liver failure, 7.5 years post transplant and 1 death from bleeding oesophageal varices at six weeks. Two patients with severe CFRLD underwent lung/liver transplantation, and are both well at 1.5 and 4.5 years post transplantation.

CF patients with pre-existing liver disease at assessment do not have significantly different survival post transplantation and liver disease does not progress in the majority of patients.